

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Impact of Sex Work on Risk Behaviors and their Association with HIV Positivity among People Who Inject Drugs in Eastern Central Canada: Cross-Sectional Results from an Open Cohort Study
AUTHORS	Campeau, Laurence; Blouin, Karine; Leclerc, Pascale; Alary, M; Morissette, Carole; Blanchette, Caty; Serhir, Bouchra; Roy, Elise

VERSION 1 – REVIEW

REVIEWER	Gabriela Paz-Bailey Team Lead for Epidemiology Centers for Disease Control and Prevention, Atlanta, Ga, United States
REVIEW RETURNED	09-Oct-2017

GENERAL COMMENTS	<p>This is an important study documenting higher risk of HIV infection among male and female persons who inject drugs and exchange sex for money compared to persons who inject drugs who do not sell sex. The authors chose to stratify the analyses by gender, which makes sense, but also by sex work status, which distracts from the argument that sex workers are at a higher risk of HIV infection. The authors should rethink their analyses strategy and justify their approach in the introduction and methods. It is not clear from the findings why a stratified analyses by sex work was needed. The prevalence of sharing syringes and injection material is high for both sex workers and non sex workers and the findings on factors associated with HIV are similar for both groups with the exception of recent incarceration. Variables such as injection partners, using syringes already used by someone else, and injecting with materials already used by someone else are equally prevalent in both groups and seem to be associated with HIV in both groups. The difference seems to be in who they share with (strangers versus known persons), but the findings on type of person they share with are inconsistent for syringes and injection materials. The relevance of this classification (strangers versus known persons) is also unclear. The discussion does not seem to be based on the results and needs greater focus and strengthening. For example, in the first paragraph of the discussion the authors argue that homelessness increases the risk of HIV as shown in other studies, but this variable was not presented for the analyses among women and is actually protective in the analyses among men. The association between homelessness and lower HIV prevalence among men may be because diagnosed HIV-positive persons may have access to housing.</p>
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	<p>The authors argue the data showed differences between sex workers and non sex workers but they do not explain how. The results do not seem to support this assertion. The authors also argue that it was more injection risk than sexual risk that were risk factors for HIV, but the sexual risk variables are limited to condom use. The outcome includes both past and recent HIV infections, and potentially most HIV-positive participants have been previously diagnosed with HIV. The authors acknowledge this limitation. However, they are not consistent in the interpretation of factors associated with HIV as risk factors for infection or a consequence of knowing your HIV-positive status. The injection risk variables are interpreted as a cause of the higher HIV prevalence and the higher condom use as a consequence of knowing ones status. A more consistent approach on the interpretation of results should be taken. If there is information on what percentage were aware of their status that information should be included in the results and used consistently in the interpretation of findings. PWID who sell sex have a higher prevalence of HIV, they are sharing injection equipment and having sex without condoms and should be prioritized for testing and linkage to care (data on how many are on ARV would be useful). Among men who sell sex, MSM have an even higher prevalence and should be another group of focus for prevention. These points need to be more clear in the discussion.</p> <p>Minor comments Acronyms should be defined in abstract.</p>
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REVIEWER	Apiradee Lim Faculty of Science and Technology, Prince of Songkla University, Pattani Campus, Muang, Pattani, 94000
REVIEW RETURNED	17-Oct-2017

GENERAL COMMENTS	<p>This manuscript provides a good discussion and can be accepted for publication.</p> <p>Comments Abstract</p> <ol style="list-style-type: none"> 1. The abbreviate words such as SWs, PWID-SWs, HCV and SurvUDI especially in the abstract should be specified full words before mention in any other places in the text. <p>Methods</p> <ol style="list-style-type: none"> 1. Are 785 subjects excluded in the analysis different from those included in the analysis? If yes, the authors should explain more. 2. Sentences in this section which had already been done should be in past tense. 3. What is the unit of analysis, number of visits or number of subjects? The authors should explain more clearly. 4. The authors should explain more about data structure used in this study. What variables are from visit table and what variables are from individual subject table? 5. Why Pearson's chi-squared and two-sample t-test were used for univariate analysis whereas GEE was used for multivariable analysis? Were these methods used the same dataset? (chi-squared and two-sample t-test are for independent observations whereas GEE are for non-dependent observations.)
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	<p>6. Please use the consistency word either cut-off or cutoff.</p> <p>7. The explanation in line 22-27 page 6 should be specified more clearly. Do the authors mean HIV negative for the sentence "Sample were considered negative..."?</p> <p>8. The total number of subjects and number of visits should be mentioned in the methods part.</p> <p>Discussion</p> <p>1. The objectives of this study shouldn't be mentioned again in this part as they are mentioned already in introduction part.</p> <p>2. Line 23, page 10 SW in the text should be SWs</p>
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VERSION 1 – AUTHOR RESPONSE

REVIEWER #1

1. Reviewer #1 suggested that the acronyms should be defined in the abstract.

Response: The following acronyms have been defined in the abstract: human immunodeficiency virus (HIV), participants who injected drugs and engaged in sex work (PWID-SW), sex work (SW).

2. Reviewer #1 suggested that the analysis strategy should be further justified in the introduction and methods to clarify why analyses stratified by sex work were needed. It was mentioned that the results did not seem to support the assertion that the data showed differences between sex workers and non-sex workers. For instance, the Reviewer noted that the prevalence of sharing syringes and injection material is high for both sex workers and non-sex workers and the findings on factors associated with HIV are similar for both groups with the exception of recent incarceration. It was also noted that variables such as injection partners, using syringes already used by someone else, and injecting with materials already used by someone else are equally prevalent in both groups and seem to be associated with HIV in both groups.

The research question for this study was formulated after an article published in 2011 by Roy et al. documented the emergence of sex work as an independent risk factor for HIV infection among PWIDs in Eastern Central Canada (Roy et al. 2011 AIDS 25(15):1897-903), thus highlighting the need for more evidence on the association between HIV infection, injection drug use and sex trade involvement.

The choice to stratify according to involvement in sex work was motivated by our initial hypothesis that the emergence of sex work as a risk factor for HIV infection was partially due to sexual behaviours, especially among men reporting sex work and sex with men.

Therefore, in response to this comment, we have explicitly stated our initial hypothesis: "We hypothesized that, in addition to injection behaviours, risky sexual behaviours would be associated with HIV positivity, especially in men reporting sex work and sex with men." (Page 3, lines 48-51).

Furthermore, while the results presented in the result section already highlights several differences between sex workers and non-sex workers, we also further emphasized the differences observed between sex workers and non-sex workers for HIV positivity correlates, especially with regard to sexual behaviours.

As stated in the section, female sex workers were more likely to be HIV-positive, to have HCV, to have been incarcerated, to have been homeless in the past six months, to report injection with a syringe and other material used by someone else that had mainly been obtained from strangers, to inject mainly with strangers, to report having lent used syringes, to have been injecting for at least six years, to report at least 120 injections in the past month, to report cocaine as their most often injected drug as well as the consumption of crack/freebase other than by injection, to report consistent condom use for vaginal and anal intercourse, to have used condoms at the last sexual intercourse and, finally, to report more than 21 male sexual partners (Page 6, lines 24-44). Some differences in correlates of HIV infection between female sex workers and non-sex workers are also noted in the result section. Factors associated with HIV infection among sex workers but not among non-sex workers include recent incarceration, injection for at least six years, injection with syringes obtained mainly from known persons and not having lent used syringes to others (Page 7, lines 41-48). Having had only oral sex was also correlated with HIV positivity among female SWs only, which has been added to the result section in response to this comment (Page 7, line 48).

Among men, sex workers were more likely to be HIV-positive, to report having been homeless in the past six months, to have injected with a syringe and other material used by someone else mainly obtained from strangers, to have injected mainly with strangers, to have lent used syringes to others, to have injected at least 120 times in the past month, to report cocaine as their most often injected drug, to use crack/freebase other than by injection, to not use condom consistently, to not have use condoms at the last sexual intercourse, to have only male sex partners or have both male and female partners and, lastly, to have had at least 21 male partners in the past six months (Page 6, line 47 to Page 7, line 22). Additionally, injection with material (other than syringes) mainly obtained from known persons was noted as a difference in correlates of HIV infection between male sex workers and non-sex workers (Page 8, lines 14-16). Finally, condom use at the last sexual intercourse as well as having both female and male sexual partners as correlates of HIV infection among male SWs were added to the result section in response to this comment (Page 8, lines 24-32).

3. The Reviewer mentioned that the relevance of the classification between strangers and known persons is unclear.

The decision to distinguish between strangers and known persons is based on a literature review of risk factors for HIV infection among PWIDs. An article by Hankins et al. published in 2002 (*J Acquir Immune Defic Syndr.* 15;30(5):514-21) showed that PWIDs from our cohort who had injected at least once in the past six months with borrowed used needles were more likely to be infected, particularly if these were obtained mainly from strangers (AOR, 1.6; 95% CI, 1.3–2.1). Additionally, an article published by Rondonelli et al. (2011 *Drug and Alcohol Dependence* 104: 167-74) showed that PWIDs whose most frequent injection partner was 'Acquaintance, stranger, drug dealer, or other' were 3.36 times more likely to be HIV-positive than those who reported the most frequent injection partner to be a 'shooting partner, friend, or relative'. In response to this comment, we added a reference to an article from this cohort referring to these two studies to the following sentence: 'Potential correlates of HIV positivity were identified based on a literature review and on previous analyses on this cohort' (Page 4, lines 35-36).

To add further clarification, the category 'strangers' was created by including casual sex partners, clients and commercial sex partners (as a client) that the participant did not know well, as well as other people (excluding sexual partners) that the participant did not know or did not know well. As for the category 'known persons', it was created by including regular sex partners, well-known casual sex partners, well-known clients and commercial sex partners (as a client) who were well known, as well as family members and close friends.

4. Reviewer #1 pointed out that in the first paragraph of the discussion, it is argued that homelessness increases the risk of HIV as shown in other studies, but this variable was not presented for the analyses among women and is actually protective in the analyses among men. The Reviewer suggested that the association between homelessness and lower HIV prevalence among men may be because diagnosed HIV-positive persons may have access to housing.

In response to this comment, the following sentence has been removed from the discussion: 'which has been shown to be associated with higher HIV infection rates among vulnerable populations, including PWIDs' (Page 9, lines 32-35). The following sentence has been added: '□...□ homelessness was associated with lower HIV prevalence among men. Considering that a large majority of participants are aware of their status, this result can be interpreted as a higher access to housing subsidies and social programs for people living with HIV, as suggested in a previous study among low-income U.S. urban residents (Dickson-Gomez et al. 2011 Subst Abuse Treat Prev Policy 6:31) (Page 9, lines 28-32).

It should also be noted that this variable was not presented among women because it did not reach the threshold in univariate analysis to be included in multivariate analyses (a p-value ≤ 0.20 in the univariate analysis was considered for inclusion in the multivariate analyses).

5. The Reviewer noted that the sexual risk variables were limited to condom use, thus questioning the validity of the assertion that it was more injection risk than sexual risk that were risk factors for HIV.

While a large numbers of sexual risk variables were examined during the preliminary phase of the study, only variables with a p-value ≤ 0.20 in the univariate analyses were considered for inclusion in the multivariate analyses. In addition, the final multivariate analyses included only significant variables (p-value < 0.05) and confounders, i.e. variables changing prevalence ratios by more than 10% when removed from the complete model. As a result, the sexual behaviors kept in the model are limited to condom use at the last sexual intercourse, consistent condom use, reporting casual sex partners, and sex of sexual partners.

In the manuscript, most of these variables were already mentioned but a few were missing, thus we completed the list (Page 4, lines 49-50, and Page 5, lines 9-10).

The following sentence has also been added to the discussion for further clarification: 'Despite having examined a variety of sexual risk behaviors for inclusion in our models □...□' (Page 9, line 49-50).

6. Reviewer #1 mentioned that the interpretation of factors associated with HIV should be more consistent, and that the percentage of participants aware of their status should be included in the results and used consistently in the interpretation of findings, as well as the percentage of participants on ARVs. For instance, the injection risk variables are interpreted as a cause of the higher HIV prevalence and the higher condom use as a consequence of knowing one's status.

In response to the first issue about consistency of the interpretation, we further clarified the possibility of reverse causality by modifying the following paragraph, which now reads: 'More positively, our results show positive associations between HIV positivity and not lending used syringes as well as consistently using condoms. A plausible explanation for these associations would be reverse causality, i.e. our results suggest that HIV-positive PWIDs might adopt behaviors to protect others. This interpretation is reinforced by the fact that a large majority (78.7%) the HIV-positive participants of this study were aware of their HIV positive status and by previous research suggesting that HIV-positive individuals who are aware of their own serological status tend to adopt protective behaviors' (Page 10, lines 25-35).

As suggested by the reviewer, the following sentence has also been added to the first paragraph of the result section: 'Among the HIV-positive participants, including both sexes as well as SWs and non-SWs, 78.7% were aware of their status. Among those, 87.9% had consulted a doctor about HIV in the past six months, and 59.3% were on antiretroviral therapy (ART)' (Page 6, lines 16-21).

The percentage of participant aware of their status has also been used more consistently throughout the discussion, with the following sentences being included: 'Interpretation of findings should take into account that the large majority (78.7%) the HIV-positive participants of the SurvUDI network for the 2004-2016 period were aware of their status' (Page 9, lines 23-25), 'Considering that a large majority of participants are aware of their status' (Page 9, lines 29-31).

7. The Reviewer suggested to clarify in the discussion that PWID who sell sex have a higher prevalence of HIV, are sharing injection equipment and having sex without condoms. They should be prioritized for testing and linkage to care.

In response to this comment, the following sentences have been added to the discussion: '□...□ including higher HIV prevalence among the former' (Page 9, line 41), 'and highlighting the need to prioritize, fund and support services to improve prevention services and linkage to care for this specific sub-group' (Page 9, lines 43-45).

8. Reviewer #1 suggested to make it clearer in the discussion that among men who sell sex, MSM have an even higher prevalence and should be another group of focus for prevention.

To add clarification, the following sentences have also been added to the discussion:

'These findings confirm our hypothesis that risky sexual behaviors would be associated with HIV positivity among PWID-SWs who have sex with men. This group has a very high HIV prevalence and should be an important focus for intervention' (Page 10, lines 15-18).

REVIEWER #2

Reviewer #2 did not suggest any modification to the manuscript.

VERSION 2 – REVIEW

REVIEWER	Gabriela Paz-Bailey US Centers for Disease Control and Prevention, Atlanta, Ga
REVIEW RETURNED	18-Dec-2017

GENERAL COMMENTS	I thank the authors for addressing my comments. This is an important contribution to the literature. I have no further comments.
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REVIEWER	Apiradee Lim Faculty of Science and Technology, Prince of Songkla University, Pattani Campus, Thailand
REVIEW RETURNED	04-Dec-2017

GENERAL COMMENTS	Can be accepted for publication
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